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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/173,864	10/16/98	IVARIE R	24011 0002

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EXAMINER	
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ART UNIT	PAPER NUMBER
1633	10

DATE MAILED: 12/22/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/173,864	IVARIE et al
Examiner	**Group Art Unit**
SUMESH KAUSHAL	1633

☒ Responsive to communication(s) filed on *Aug 29, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *19, 21, 25, 27, 29, 33-35, and 41-57* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *19, 21, 25, 27, 29, 33-35, and 41-57* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The applicant's response filed on Paper No. 8, 8/29/99 has been fully considered. Claims 25, 27, 35, 50, 53-54 are amended. Newly filed claims 55-57 are entered. Claims 19, 21, 25, 27, 29, 33-35, 41-57 are pending in this application. Applicant's arguments filed on Paper No 8 have been fully considered but they are not persuasive in view new grounds of rejections below.

Claim Rejections - 35 USC § 112

1. Claims 19, 21, 25, 27, 29, 33-35, 41-57 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, **had possession of the claimed invention.**

The instant claims are drawn to a transgenic birds (chicken and turkey) wherein the exogenous transgene is expressed in the tubular gland cells of the avian oviduct wherein the constitutive promoter is CMV promoter. Claims are also drawn to a method of producing an avian egg from a transgenic avian which contain exogenous protein where in the proteins secreted into the oviduct lumen so that the protein is deposited on the yolk of an egg. Claim is also drawn to the method of producing an egg wherein the vector used to make transgenic avian encodes two coding sequences wherein the second coding sequence is capable of providing post translational modification of the protein encoded by the first coding sequence, wherein an internal ribosome entry site element (IRES) is positioned between first and second coding sequence. Claims are also drawn to a method of producing an exogenous protein in avian oviduct by making a transgenic avian (as claimed) wherein the protein is expressed in tubular gland cells of transgenic avian. Claims are also drawn to a

transgenic bird having transgene in the genetic material of the tubular gland cells of it magnum and the transgene is expressed in the tubular gland cells of the transgenic bird. Claims are also draw to the transgenic bird expressing exogenous gene in the tubular gland cells of its magnums wherein the protein is deposited in eggs of that bird. In addition claims are drawn transgenic avian and eggs wherein the exogenous protein is interferon.

Applicant is referred to the Interim guidelines on **Written Description** published June 15, 1998 in the Federal Register, Vol. 63, No. 114, pp. 32639-32645 (also available at www.uspto.gov). In analyzing whether the written description requirement is met for the claimed invention, it is first determined whether a representative number of species have been described by their complete structure (it is not realistic to expect that the "complete structure" of an animal, or even a cell, could be described. Therefore, the inquiry required by this portion of the written description guidelines is interpreted to be whether the phenotypic consequences of altering the genotype have been described).

In this case, the few disclosed embodiments are not representative of the products claimed. The claims encompass a transgenic birds and transgenic eggs obtained from the transgenic birds. Birds encompass a huge genera of avian species including Crow, Ostrich, Eagle, Turkey and Sparrows etc. The specification disclosed only a transgenic chicken. Next, it is then determined whether a representative number of species have been sufficiently described. The specification disclosed only a chimeric chicken (White Leghorns) and fails to described any and all the claimed transgenic birds (as claimed). The specification fails to describe the claimed products because chimeric chickens and eggs are not predictive of any and all the transgenic birds and eggs. The limited disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of any and all transgenic birds and eggs obtained from them at the time the application was filed. Thus, it is concluded that the written description requirement is not satisfied for the claimed invention.

2. Claims 19, 21, 25, 27, 29, 33-35, 41-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to **make and/or use the invention**.

The specification teaches making of an ALV-base retroviral vector wherein the CMV promoter derives the expression of b-lactamase (example-1 and 2). The specification teaches production of chimeric chickens transducing stage X embryos with NLB-CMV-BL retroviral particles (page 34, line 10-15). The specification further teaches the detection of b-lactamase activity in the egg white of chimeric chickens (page 36 table-1). However, the specification fails to show even a single transgenic founder obtained from chimeric chickens, capable of producing a transgenic progeny expressing the b-lactamase activity in oviduct and/or eggs in any and all offsprings. The transgenic animals by definition are animals with exogenous DNA integrated in the germ cells and are capable of transmitting the trait to their progeny. The art at the time of filing teaches that germ line transmission using chimeric birds has been unpredictable (Sang TIBTECH 12:415-420, 1994, see page 416, col.1 para.3). Furthermore, ex-vivo transfection of blastodermal cells and reimplantation into an egg has not show to transmit the transgene through germ lines (Sang page 417, col.1 para. 1). Furthermore, the specification fails to provide a clear correlation between working examples and the desired oviduct-specific expression of an exogenous protein in any and all transgenic avian with a reasonable expectation of success. The state of the art at the time of filing was such that replication defective retroviral vector has been used to obtain germ line transmission of transgenes resulting in a wide variety of tissues, however tissue-specific expression has not been achieved (Simkiss, Transgenic birds, animals with novel genes, Mclean ed, Cambridge Univ.Press NY pages 106-137, 1994, see paragraph bridging pages 118-119). The specification fails to show the expression of any exogenous protein (as claimed) in the tubular gland cells of oviduct or magnum tissue of any and all birds. The specification only provided a prophetic example in fig-6 which illustrates magnum-specific

gene expression in magnum and non-magnum cells (page 13, line 9-13). The specification only teaches the detection of b-lactamase in egg white and fails to demonstrate it expression in oviduct magnum tissue (page 36, table-1). Furthermore, the specification does not enable one skill in the art to determine the control elements required for directing the synthesis of a transgene product into egg white or onto egg yolk. The specification fail to provide guidance to one of skill to determine signal sequences that direct a protein to egg white or egg yolk because yolk proteins require specific internal recognition sequences for uptake into yolk (Sang, page 418, col.2, para. 3). In addition the specification fails to teach the making of a transgenic avian capable of expressing interferon in the tubular gland of the avian oviduct and into an egg. Considering the unpredictability in tissue specific transgenic art the specification does not even provides a single working example wherein any and all exogenous proteins (as claimed) are expressed in the oviduct of any and all birds.

Furthermore, the method of providing post-translational modification of the proteins deposited in an avian egg is not enabled because specification fails to provide guidance to the claimed method of post-translational modification of any and all proteins deposited into an egg. The specification even fails to teach the claimed genetic construct encoding a protein, an IRES element and a second encoding sequence required for post-translational modification. The specification only states the first coding sequence may encode collagen which would be hydroxylated and made active by an enzyme encoded by the second coding sequence but fail to provide even a single working example, wherein after post-translational modification any and all protein(s) are deposited in an egg (see page 23 lin 23, App. Spec). The state of the art at the time of filing was such that various factor affects the extent of the post translational modification of proteins. For example, besides the type of enzyme used for the post translational modification of collagen, one of the critical factor that regulates the collagen post-translational modification is the ratio of enzyme to substrate in the cell. (Myllya et al, Biochem. J. 196:683-692, 1981, see page 691, col.2 lin.1). The specification fails to provide guidance to a specific modulating enzyme for post translational modification of collagen or

any other protein of interest and fails to show the claimed post translational modification of a protein. The instant invention is the method of producing an egg containing post-translationally modified exogenous protein and not to the transformed chicken fibroblasts as demonstrated by Myllya et al. Furthermore, the specification fails to show the deposition of any and all exogenous protein in an avian egg, which is post translationally modified using the claimed di-cistronic vector, encoding any and all proteins and any and all modifying enzymes. This is further evident from applicants response that "the precise regulation of post-translational modification of many native proteins in cells is very complex" (Paper 8, page 10, line13), which renders the claimed invention more unpredictable where an exogenous protein is deposited into an egg after post-translational modification (as claimed). Thus, considering the state of the art at the time of filing and the lack of working examples provided in the specification, the skilled artisan at the time of filing would be lacking a reasonable expectation of success, to make a transgenic avian capable of delivering an egg containing the post translational modified exogenous protein, without excessive an undue amount of experimentation.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 50 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims recite a second coding sequence capable of providing post translational modification of a protein encoded by first coding sequence. The instant claim fails to recite the protein encoded by first coding sequence and the enzyme required for its post translational modification encoded by the second coding sequence.

Claim Rejections - 35 USC § 102

4. Applicant's arguments filed on Paper No. 9, pages 13-14 are persuasive. Rejection of claim 27 and 33 under 35 U.S.C. 102(b) has been withdrawn.

5. Applicant's arguments filed on Paper No. 9, pages 14-15 are persuasive. Rejection of claims 19, 21, 25, 27, 29, 34, 35, 41, 42, 44, 47 and 51-54 has been withdrawn under 35 U.S.C. 102(e).

Claim Rejections - 35 USC § 103

6. Applicant's arguments filed on Paper No. 9, pages 15-18 are persuasive Rejection of claims 43, 45, 46, 48 and 49 under 35 U.S.C. 103(a) has been withdrawn.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jasemine Chambers Ph.D. can be reached on (703) 308-2035. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-2035. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

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